REMARKS/ARGUMENTS

Claims 1-20 are pending in the application, of which claims 7, 13, 14, and 18-20 were withdrawn from consideration, and claims 1-6, 8-12, and 15-17 have been rejected. Claims 1, 2, 4, 6, and 15 have been amended herein. Support for the amendments can be found, for instance, within the original claims.

Information Disclosure Statement

Applicants acknowledge the Examiner's discouragement of using copies of previous information disclosure statements and the potential to confuse the record. Applicants are preparing a new IDS containing the references cited in previous IDSs.

OBJECTIONS:

Sequence Compliance

The Examiner indicated that the application fails to comply with the requirements of 37 CFR 1.821 - 1.825 as the specification discloses sequences that are not accompanied by the required Sequence Identifiers. Accordingly, Applicants have amended the specification to include such identifiers, thus obviating this rejection.

Specification

The Examiner has objected to the Specification for a number of minor informalities. Accordingly, Applicants have amended the specification, thus obviating these objections. Furthermore, the title of the invention has been amended to more accurately describe the present invention, as required by the Examiner.

In section 2e of the Office Action, the Examiner has objected that the specification contains references to Figures that were deleted in the amendment of 16 January, 2004. Applicants are reconsidering re-introducing these Figures into the application. Pending resolution of this matter, Applicants request the Examiner to hold this objection in abeyance.

Claims

The Examiner has objected to the claims for some minor informalities. Accordingly, Applicants have amended the claims to render these objections moot.

REJECTIONS:

35 U.S.C. 101 and 35 U.S.C. 112, first paragraph (enablement)

Claims 1-6, 8-12 and 15-17 stand rejected for alleged lack of utility. The Examiner makes a general allegation that novel biological molecules lack well established utility. The Examiner acknowledges that the specification clearly identifies uses of CLASP-2, by identifying that CLASP-2 is involved in a variety of cellular processes, such as immune function, T cell activation, and regulation of T cell and B cells. The specification also discloses that CLASP-2 and CLASP-2 regulators can be used to treat, detect, or modulate immune system disorders, hematopoietic cell disorders, allergic reactions, organ rejection or graft-versus-host disease, inflammation, infectious agents. However, the Examiner alleges that these asserted utilities are not substantial, since they are not present in mature form and readily used in a real world sense.

Among other things, the Examiner asserts that significant further research is allegedly needed "to determine how" CLASP-2 is involved in such processes. *Office Action at page 7.* Applicants submit that knowledge of how an invention works is not needed for patentability. It is enough for Applicants to have identified that CLASP-2 is in fact involved in such processes, and to have identified the diseases states that ultimately correlate with CLASP-2 dysfunction.

The Examiner further asserts that there is a lack of evidence that CLASP-2 is involved in T-cell activation. The specification allegedly does not disclose an actually observed correlation of a disease state with a mutated, deleted, or translocated or altered levels of a CLASP-2 gene, or provide evidence that manipulating CLASP-2 will affect any of these diseases.

As the Examiner has acknowledged, however, the specification clearly identifies that CLASP-2 is involved in immune-response processes such as T cell activation. Moreover, CLASP-2 is a member of a family of highly similar proteins. The application discusses how

another member of the same family called CLASP-1 has been confirmed to be involved in T-cell activation: for instance, antibodies to the extracellular domain of CLASP-1 also block T-B cell conjugate formation and T cell activation (*see paragraph 6 of the published application*). The application also emphasizes the striking sequence similarity between CLASP-1 and CLASP2 (*see, for instance, Figure 5 of the application*).

Finally, post-filing work has confirmed the involvement of CLASP-2 in immune response, especially T-cell activation. Multiple publications have shown that CLASP-2 (also called Zizimin 1 or DOCK9) interacts with and activates a rho-family GTPase called cdc42. (*See, e.g*, Meller et al., Nat Cell Biol. 4(9):639-47 (2002 Sep), *copy attached*). Activated Cdc42 in turn promotes cyoskeletal polarization in T cells in response to contact with antigen-presenting cells. (*See, e.g.*, Stowers et al., PNAS USA Vol 92: pages 5027-31, (1995) , *copy attached*). The role of CLASP-2 in promoting T-cell activation is of clear relevance to immunological diseases such as immune system disorders, allergic reactions, organ rejection, etc.

Under Section 2107, Part II of the MPEP, the burden is on the Examiner to establish that it is **more likely than not** that a person of ordinary skill in the art would not consider Applicant's utility to be specific and substantial. Among other things, the Examiner is required to provide scientific reasoning and **support for factual findings** relied upon in reaching this conclusion.

At the very least, the very striking sequence similarity between CLASP-1 and CLASP-2 imparts substantial credibility to Applicants' assertion that CLASP-2 (like CLASP-1) is involved in T-cell activation. There is absolutely no basis for the Examiner to argue to the contrary or to assert that Applicants' disclosed utility of CLASP-2 is neither specific nor substantial. The Examiner needs to establish that it is more likely than not that CLASP-2 does not have a similar utility to CLASP-1 in order to establish a prima facie case of lack of utility. The Office Action falls far short of meeting this burden.

Although the diseases identified by Applicants may have complex mechanisms, their pathologies are mediated at least in part by T cell activation. As discussed above, postfiling evidence has confirmed Applicants' statements that CLASP-2 is involved in T cell activation. Although it is possible that compounds identified by the claimed methods are unlikely to

completely cure or prevent such diseases, inhibiting devolvement of one aspect of their pathology, *i.e.*, T cell activation, is highly likely to be of some clinical benefit to a patient with such a disease. This is a perfectly sufficient basis for utility.

"Courts have repeatedly found that the mere identification of a pharmacological activity of a compound that is relevant to an asserted pharmacological use provides an "immediate benefit" and thus satisfies the utility requirement. MPEP § 2107.01. "Knowledge of the pharmacological activity of any compound is obviously beneficial to the public. It is inherently faster and easier to combat illnesses and alleviate symptoms when the medical profession is armed with an arsenal of chemicals having known pharmacological activities.

The Office Action's allegation that it is necessary to completely characterize the nature of CLASP-2's involvement in T cell activation is incorrect. Nor is in necessary for Applicants to disclose actual working examples of inhibitors. Inhibitors can be identified by the relatively simple in vitro binding assays disclosed in the specification. The specification provides detailed teaching on how to identify such inhibitors. For example, various in vitro and in vivo assays to detect T cell activation and to assay immunological diseases such as rejection and autoimmune diseases are set for at paragraphs 384-428 of the specification. Examples 7A and 7B disclose assays for CLASP-2 inhibitors. It is not necessary to have a complete understanding of underlying mechanisms to identify inhibitors of CLASP-2 activity, nor to perform trials of such identified inhibitors in cellular or animal models for activity in protecting against cells death. It can be agreed that after inhibitors of CLASP-2-activity have been identified they would need to be subject to further screening in, for example, cellular or animal models and clinical trials, before any therapeutic use. However, such is by definition the case for any primary screening method for a pharmaceutical, and does not imply a lack of patentable utility. Usefulness in patent law, and in particular in the context of pharmaceutical inventions, necessarily includes the expectation of further research and development. *In re Brana*, 34 USPQ2d 1436 (Fed. Cir. 1995).

Because it is highly credible that the claimed methods will result in identifying compounds have a pharmacological activity (*e.g.*, inhibiting T cell activation) which is relevant to various diseases disclosed in the specification, the claimed methods have patentable utility.

Under these fact, Applicants submit that the application sets forth a utility for CLASP-2, and that the Examiner has provided no plausible reasoning, let alone factual support, for asserting otherwise. As mentioned, the burden is on the Examiner to establish her assertion by a preponderance of the evidence, a standard that the Examiner has not met in any way. Applicants accordingly request that this rejection be withdrawn.

35 U.S.C. 112, first paragraph (lack of possession)

Claims 1-6, 8-12, and 15-17 are rejected under 35 USC 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Claim 5 is rejected on similar grounds.

The basis for this rejection appears to be an alleged lack of possession for sequence variants and/or fragments of SEQ ID NOs:1 and 2. Since Applicants have amended to claims to recite polynucleotides comprising a nucleic acid encoding SEQ ID NO:2, this rejection is rendered moot.

In addition, the Examiner required a deposit of cDNA clones of CLASP-2 to be made in order to satisfy the requirements of Paragraph 112. The Examiner has noted that the specification mentions that cDNA clones of the claimed sequences have been deposited, (pg 110, lines 31-34; pg 111, lines 1-9 of the specification). The Examiner has requested Applicants to supply an affidavit or declaration stating that the clones will be made available to the public upon the issuance of a patent. In response, Applicants have supplied such a Declaration (copy attached).

35 U.S.C. 112, second paragraph

Claims 1-6, 8-12, and 15-17 are rejected under 35 USC 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention.

More specifically, the Examiner indicates that claims 1-6, 8-12, and 15-17 fail to define the metes and bounds of the varying structures of polynucleotides recited in the claimed methods. This rejection appears to be based on claim language directed to sequence variants and/or fragments of SEQ ID NOs:1 and 2. Since Applicants have amended to claims to recite polynucleotides comprising a nucleic acid encoding SEQ ID NO:2, this rejection is rendered moot.

35 USC 102 - anticipation

Claims 1 and 15-16 are rejected under 35 USC 102(a) as being anticipated by Pianese et al.

This rejection has been rendered moot by Applicants' amendment to the claims to recite polynucleotides comprising a nucleic acid encoding SEQ ID NO:2. Pianese et al. does not disclose or suggest such a sequence.

35 USC 103 - obviousness

Claims 8-12 and 17 are rejected under 35 USC 103(a) as being unpatentable over Pianese et al., in further view of Jacobs et al.

This rejection has been rendered moot by Applicants' amendment to the claims to recite polynucleotides comprising a nucleic acid encoding SEQ ID NO:2. Pianese et al. does not disclose or suggest such a sequence. Jacobs does not remedy this deficiency.

CONCLUSION

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 650-326-2400.

Respectfully submitted,

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Attachments:

1) Exhibit A - Stowers et al., "Regulation of the polarization of T cells toward antigen-presenting cells by Ras-related GTPase CDC42" *Proc. Natl. Acad. Sci. USA*, Vol. 92 (May 1995), pp. 5027-5031; and

2) Exhibit B - Meller et al., "CZH proteins: a new family of Rho-GEFs" *Journal of Cell Science* 118 (2005), pp. 4937-4946.